

REMARKS

The Office Action and the cited and applied reference have been carefully reviewed. No claim is allowed. Claims 19, 21-23, 25, 28, 31-36, 40, 41, 43-45, 48, 50, 53-55 and 57-62 presently appear in this application, with claims 33-36 withdrawn by the examiner, and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Non-elected claims 37-39 are cancelled without prejudice to refiling in a divisional application.

As applicants believe that the obviousness rejection over the cited Kovalovich reference is obviating by the arguments presented below, consideration of claims 33-36, directed to a nonelected species, is respectfully requested.

The telephonic interview between the undersigned and Examiner Mertz on December 16, 2008, is gratefully acknowledged. As indicated on the interview summary mailed December 17, 2008, the scope of enablement rejection and the obviousness rejection over the Kovalovich et al. (2001) reference were discussed. During a discussion of the scope of enablement rejection, where the undersigned argued that a simple search (i.e., Google search) of CCl₄ and liver cirrhosis (to which the present claims are directed to treating instead of a generic liver injury) turns up numerous articles confirming applicants' arguments in the

amendment of August 1, 2008, that the CCl₄ model is an art accepted model for liver cirrhosis. The examiner indicated that she did not see much of a problem with this rejection but was more concerned with the obviousness rejection over Kovalovich. The undersigned argued that varying the dosage of IL-6 to less than 1% of Kovalovich's dosage would be unobvious because there is simply no expectation that such a low dose of IL-6 would be effective for the intended purpose. As the examiner remained unconvinced regarding this obviousness issue, the undersigned indicated that this rejection would be again reviewed for further arguments.

Claims 19, 21-23, 25, 28, 31, 32, 40, 41, 43-46, 48, 50, 53-55 and 57-62 have been rejected under 35 U.S.C. §112, first paragraph, because the examiner states that the specification, while being enabling for a method of inducing proliferation of hepatocytes in CCl₄ induced chemical cirrhosis, does not reasonably provide enablement for a method for treating liver injury in claim 1. The examiner takes the position that applicants' arguments are unpersuasive because even though the carbon tetrachloride/phenobarbital model is a model for impaired liver regeneration and liver cirrhosis, there are other factors that are responsible for cirrhosis, including alcohol, viruses or hereditary factors. This rejection is respectfully traversed.

Applicants agree that there are different factors responsible for liver cirrhosis. However, the present claims are not directed to preventing liver cirrhosis but rather are directed to treating liver cirrhosis regardless of what factors caused the disease. As CCl₄ induced chemical cirrhosis is an art accepted model for liver cirrhosis (as evidenced by the numerous references in the art to this animal model of liver cirrhosis) and for the study of treatment for liver cirrhosis in general, the presently claimed invention for treating liver cirrhosis is believed to be enabling to one of skill in the art.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 19, 21-23, 25, 28, 31, 32, 40, 41, 43-46, 48, 50, 53-55 and 57-62 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. This rejection is obviated by the amendment to claim 19 to recite an "effective" dose of IL-6 and by the amendment to claims 40, 41 and 55 to delete without prejudice the recitation of "expression vector".

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 19, 21-23, 25, 28, 31, 32, 40, 41, 43-46, 48, 50, 53-55 and 57-62 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Kovalovich et al., (2001), not under

§102(b) as inadvertently indicated by the examiner. This rejection is respectfully traversed.

Contrary to the examiner's assertion, Kovalovich does not teach treating liver injury with IL-6. Rather, Kovalovich describes previous studies where pretreatment with IL-6 prior to CCl₄-induced injury and apoptosis protected against liver injury (page 26605, near the bottom of the right column). Kovalovich's own experiments use a pretreatment of IL-6 20 minutes prior to intraperitoneal injection with Jo-2 mAb (an agonistic antibody to the Fas receptor which directly causes hepatic injury by stimulating the apoptotic cell death program) to determine if IL-6 exerts its protective effect on the liver through modulation of the apoptotic cell death program (page 26606, left column, first full paragraph, and sentence bridging pages 26606 and 26607). Accordingly, Kovalovich is not directed to treating with IL-6 after cirrhosis induced by CCl₄ (pretreatment is not the same as treatment after the occurrence of disease). In contrast to the present invention, Kovalovich does not administer CCl₄ to induce liver cirrhosis but instead administers Jo-2 mAb in order to induce apoptosis. Kovalovich also relies on pretreatment with IL-6 prior to the mAb treatment. Thus, Kovalovich's disclosures and teachings are concerned with prevention of apoptosis by pretreatment of genetically modified mice with IL-6, whereas the presently claimed invention is directed to treating rats with IL-

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6 only after cirrhosis has been induced with CCl₄. The fact that pretreatment of certain specifically modified mice with IL-6 can prevent or alleviate the effect of an apoptosis inducer cannot make obvious the treatment of liver cirrhosis with very low dose (less than 1% of what is used in Kovalovich) IL-6. Accordingly, Kovalovich simply cannot lead one of ordinary skill in the art to the presently claimed invention.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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